UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN 27 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: 4-CPA; 4-Chlorophenoxyacetic Acid - Acute Inhalation Toxicity Study in the Rat (§81-3)

DP Barcode: D196300 **Case:** 802264
Submission: S452154 **PC Code:** 019401
Identification No.: 019401-008906 **MRID No.:** 429682-01
Action: 627 GENERIC DATA SUBMISSION

FROM: Alan C. Levy, Ph.D., Toxicologist Alan C. Levy 1-26-94
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THRU: Jess Rowland, M.S., Acting Section Head Jess Rowland 1/26/94
Review Section IV, Toxicology Branch II
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and

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Toxicology Branch II
Health Effects Division (H7509C)

REQUEST: Review an acute inhalation toxicity study in rats with 4-Chlorophenoxyacetic Acid.

Registrant: Hunt-Wesson Inc., Fullerton, CA

EXECUTIVE SUMMARY:

In an acute toxicity study, 4-Chlorophenoxyacetic acid (4-CPA) was administered by inhalation as a dust for 4 hours to 5 male and 5 female Harlan Sprague Dawley rats. There was a 14-day post-exposure observation period. All rats survived. Ocular and nasal wetness/ encrustation were observed on the day of exposure. **The LC50 > 5.25 mg/L.**

Core Classification: Minimum

This study satisfies the data requirement (§81-3) for an Acute Inhalation toxicity study in rats.

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Reviewed by: Alan C. Levy, Ph.D. Alan C. Levy 1-26-94
Section IV, Tox. Branch II (H/509C)

Secondary reviewer: Jess Rowland, M.S. Jess C. Rowland 1/28/94
Section IV, Tox. Branch II (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute Inhalation Toxicity Study - Rats (§81-3)

TEST MATERIAL: 4-CPA; 4-Chlorophenoxyacetic acid

SYNONYMS: none

MRID No.: 429682-01 **PC Code:** 019401

STUDY NUMBER: 92N1192 Revised

SPONSOR: Hunt-Wesson Inc., Fullerton, CA

TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Chemicals and Plastics Company Inc.
Export, PA

TITLE OF REPORT: 4-Chlorophenoxyacetic Acid: Acute Dust Inhalation Toxicity Study in Rats

AUTHOR: D.J. Nachreiner

REPORT ISSUED: September 8, 1993

EXECUTIVE SUMMARY:

In an acute toxicity study, 4-Chlorophenoxyacetic acid (4-CPA) was administered by inhalation as a dust for 4 hours to 5 male and 5 female Harlan Sprague Dawley rats. There was a 14-day post-exposure observation period. All rats survived. Ocular and nasal wetness/ encrustation were observed on the day of exposure. **The LC50 > 5.25 mg/L.**

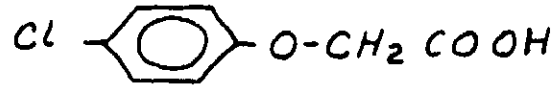
Core Classification: **Minimum**

This study satisfies the data requirement (§81-3) for an Acute Inhalation toxicity study in rats.

I. TEST ARTICLE

Name: 4-CPA; 4-Chlorophenoxyacetic acid

Formula:



Purity: 99.8% by weight
Reference No.: 89F002125
Sample No. (Bushy Run No.): 56-39
Appearance: white powder
Particle Size: 86.03% between 1 and 3 microns

II. METHODS AND MATERIALS

A. Statistical Analyses

No[illegible] were made.

B. Regulatory Compliance

A good Laboratory Practice Compliance statement, Quality Assurance statement and a list of Quality Assurance inspections were included in the Report.

A statement of "no claim of confidentiality" was included in the Report.

C. Animals

Sprague Dawley albino rats of both sexes were received from Harlan Sprague Dawley, Inc., Indianapolis, IN. They were 42 days old when received from the supplier and 62 days old at the time of exposure. The rats were housed 5/cage during the nonexposure times and individually during exposure (wire mesh cages). Temperature and humidity were "routinely maintained" at 66-77°F and 40-70%, respectively. There was a 12 hour light/dark cycle. Food and water were available ad libitum except during the 4-hour exposure period. Rats were assigned to the exposure group by a "card-based randomization method." Exposure day body weights were 248-270 g for males and 178-198 g for females.

D. Exposure

The 4-hour exposure period was from the time the generation system was turned on until it was turned off. Study day 0 was the day of exposure and the 14-day post-exposure period was study days 1 through 14. There was no air-only control exposure group.

E. Inhalation Chamber

The plexiglas and stainless steel chamber was 0.38 x 0.52 x 0.61 m and had a volume of about 120 L. The airflow was 32 L/min (16 changes/hour). The time required for the chamber to reach 99% of the target concentration was calculated to be 17.3 min (t99).

F. Dust Generation

Dust atmosphere was generated with a stainless steel auger-type dust feed. The dust was carried by a venturi-generated air stream to the chamber inlet where a baffle and countercurrent airflow dispersed the dust throughout the chamber. A vacuum line removed the air from the chamber.

G. Chamber Atmosphere Measurements

Gravimetric methods were used to analyze chamber concentrations of particulates. About 4.0 L/min was the sample flow rate. Eight samples (2 minute collection time) were taken during the 4-hour exposure. The nominal concentration was calculated by dividing the weight of the test substance by the air volume which passed through the chamber.

Particle size distribution was measured twice and the mass medium aerodynamic diameter (MMAD) and geometric standard deviation were obtained. These were used to calculate D16 and D84 values. Temperatures and humidity of the chamber were recorded.

H. Observations and Measurements

Rats were observed about every 30 minutes during the 4-hour exposure period and findings were recorded on a group basis. Detailed individual exams were made after exposure and each morning for the 14 days post-exposure. In addition, they were observed each P.M. for mortality and clinical signs. Body weights were recorded just prior to exposure (study day 0) as well as on study days 7 and 14 (just prior to sacrifice). Body weight changes were calculated (day 0 from days 7 and 14).

The animals were anesthetized with methoxyflurane and exsanguinated on day 14. Complete necropsies were performed.

III. RESULTS

A. Chamber Atmosphere

1. NOMINAL CHAMBER CONCENTRATION (Report pages 23 and 24)

Gravimetric Conc. (mg/L)	Exposure Duration (min)	Chamber Airflow Rate (L/min)	Weight of Test Substance Used (g)	Nominal Concentration (mg/L)
5.25±0.231	240	32.0	43	44.7

Concentrations were measured for 2 minutes 8 times during the 4-hour exposure. They ranged from 5.729-4.906 mg/L (mean of 5.25 ± 0.231 S.D.). Report page 10 stated, "Disparity between the gravimetric [by Reviewer: 5.25 mg/L] and nominal [by Reviewer: 44.7 mg/L] concentrations is typically observed in dust studies because of the significant loss of the test substance in the generation equipment and conducting tubing to the chamber, as well as on the animals, cages, and chamber wall surfaces. Also, large particles do not remain airborne and, therefore, do not contribute to the measured exposure concentration."

2. PARTICLE SIZE ANALYSIS (Report page 25)

Gravimetric Concentration (mg/L)	Sample Number	MMAD (μ)	Geometric Std. Dev.	D16 (μ)	D84 (μ)
5.25 5.25	1 2	2.275 2.260	1.472 1.474	1.55 1.53	3.35 3.33
MEAN =		2.268		1.54	3.34

Based on particle mass distribution data, about 3.5% of the aerosol was ≤ 1 micron.

3. CHAMBER TEMPERATURE AND HUMIDITY (Report page 11)

Mean chamber temperature (± S.D.) and relative humidity (± S.D.) during exposure were 24 ± 0°C and 47 ± 0%, respectively.

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B. Animal Observations

1. MORTALITY

All 5 males and all 5 females survived until the scheduled day 14 sacrifice.

2. CLINICAL OBSERVATIONS (Report pages 14, 29 and 30)

All rats had the following:

<u>During Exposure</u> - blepharospasm and fur covered with white powder

<u>Post Exposure on Day of Exposure</u> - periocular wetness, perinasal wetness, perioral wetness, periocular (white) encrustation and powder on the fur

<u>Post Exposure (Day 1)</u> - periocular (white) encrustation

<u>Post Exposure (Days 2-14)</u> - none

3. BODY WEIGHTS (Report pages 14 and 15)

Males						Females					
Rat #	Weight g at Day			Wt gain day		Rat #	Weight g at Day			Wt gain day	
	0	7	14	0-7	0-14		0	7	14	0-7	0-14
15	266	322	357	56	91	35	184	202	212	18	28
16	248	309	345	61	97	36	187	198	206	11	19
17	255	289	320	34	65	37	178	207	215	29	37
18	270	334	361	64	91	38	181	207	218	26	37
19	262	303	326	41	64	39	198	222	243	24	45
M	260	311	342	51	82	M	186	207	219	22	33
SD	9	17	18	13	16	SD	8	9	14	7	10

M = Mean
SD = Standard Deviation

4. GROSS NECROPSY FINDINGS (Report pages 33-36)

Male 00617 - liver: anomaly, parietal surface of median lobes, near hilus, 3 mm in diameter

Female 00635 - liver: anomaly, at junction of median lobes, parietal surface, 5 mm in diameter; adhesion, anomaly adhered to diaphragm

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The above findings were not considered to be treatment related.

IV. DISCUSSION

The mean gravimetric chamber concentration was 5.25 mg/L and the nominal concentration was 44.7 mg/L. The Report indicated that the discrepancy was due to dust exposure because of a loss of the test article in equipment as well as on animals, cages and chamber walls. The mass mean aerodynamic diameter (MMAD) was 2.27 microns.

There was no mortality. Clinical signs of blepharospasm, white encrustation around the eyes, white powder on the fur and periocular, perioral and perinasal wetness were observed on the day of exposure with periocular encrustation on the day following exposure. All animals gained weight. There were no gross necropsy findings considered to be related to 4-CPA administration.

V. CONCLUSIONS

In an acute toxicity study, 4-Chlorophenoxyacetic acid (4-CPA) was administered by inhalation as a dust for 4 hours to 5 male and 5 female Harlan Sprague Dawley rats. There was a 14-day post exposure observation period. There was no mortality. Ocular and nasal wetness/encrustation were observed on the day of exposure.

The LC 50 > 5.25 mg/L.

Core Classification: Minimum

This study satisfies the data requirement (§81-3) for an Acute Inhalation toxicity study in rats.

END